

## **REMARKS**

### ***Pending claims***

Claim 1 has been amended to more clearly point out and distinctly claim the invention. Support for the phrase "water-soluble", defining the biocompatible organic multi-acid or biocompatible salt thereof, can be found on page 12, lines 4-6. After these amendments are entered, eleven (11) Claims (claims 1-11) are pending.

### **Rejections Under 35 USC 103**

Claims 1-11 were rejected under 35 USC 103(a) as being unpatentable over Stockinger et al. in view of the admitted prior art set forth in instant specification at page 2, line 22 through page 3, line 5 and British Patent 1,177,100. For the following reasons, the Examiner's rejection is respectfully traversed.

First, Applicants respectfully submit that the examiner might misunderstand the Applicants' statements in the specification from page 2, line 22, through page 3, line 5. What Applicants states is that "there have been attempts to stabilize poly(oxyalkylene)-containing materials" by using hindered phenolic compounds (antioxidants). Applicants further state that "[t]hose antioxidants may not be suitable for applications where the device is remain in contact with living tissues for long periods of times due to their cytotoxicity, or are water insoluble so that they can not be used in a water-base formulation for making the poly(oxyalkylene)-containing materials, and that "those antioxidants may not be efficient in stabilizing poly(oxyalkylene)-containing materials and/or reducing the levels of by-products such as formic acid, in case where the poly(oxyalkylene)-containing materials are used to make contact lenses or other medical devices. Applicants **do not** state that the prior art teaches the present invention, i.e., stabilizing poly(oxyalkylene)-containing materials" by using a water-soluble and biocompatible organic multi-acid or biocompatible salt thereof.

Second, Applicants submit that a *prima facie* case of obviousness has not been established. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Applicants respectfully submit that the cited secondary reference (British Patent 1,177,100) is totally different from the claimed invention. It is true that the cited reference discloses manganese citrate as one of powdered manganese or manganese compounds in stabilizing PEG (Example 7, Test 7 taught at page 6 of British – 100). But, British – 100 is directed to use of **manganese** in stabilizing PEG, whereas the claimed invention is directed to use of a water-soluble and biocompatible organic multi-acid or biocompatible salt thereof in stabilizing poly(oxyalkylene)-containing materials. This difference is unambiguously shown by the teachings of British -100 on page 1, lines 66-74

The present invention is based on the observation that stabilization of alkylene oxides and reaction products of alkylene oxides with substances containing active hydrogen can relatively simply effected by adding to them or their solutions minor amounts of **powered manganese metal** or of a **manganese-containing compound**. [emphasis added]

In fact, British -100 is totally silent about the use of a water-soluble and biocompatible organic multi-acid or biocompatible salt thereof. In addition, British – 100 does not appreciate the claimed invention, i.e., poly(oxyalkylene)-containing materials can be stabilized by a **water-soluble** and biocompatible **organic multi-acid** or biocompatible salt thereof". Without such appreciation of the invention, there is no teaching or suggestion to make the combination of the two references proposed by the examiner. Therefore, no person skilled in the art can be motivated to combine the two references and there is no reasonable expectation of success for such combination.

Even if the two references are combined, the combination still fails to suggest or teach all of the limitations of invention as currently claimed. None of the cited primary and secondary references discloses or suggests anything about use of a water-soluble and biocompatible organic multi-acid or biocompatible salt thereof in stabilizing poly(oxyalkylene)-containing materials. Manganese citrate disclosed in the secondary reference (British – 100) is not water-soluble, as shown by the attached MSDS for manganese citrate that manganese citrate is "**very slightly soluble**." Moreover, manganese citrate does not meet the definition of "biocompatible salt" as defined by Applicant on page 7, 2<sup>nd</sup> full paragraph

"Biocompatible", as used herein, refers to a material or surface of a material, which may be in intimate contact with tissue, blood, or other bodily fluids of a patient for an extended period of time without significantly damaging the ocular environment and without significant user discomfort. [Emphasis added]

As shown by the MSDS of manganese citrate, by exposure to eye, manganese can cause redness and tear production of eyes, namely causing significant user discomfort. The combination of the cited references can merely results in stabilization of poly(oxyalkylene)-containing materials by a **water-insoluble** manganese citrate.

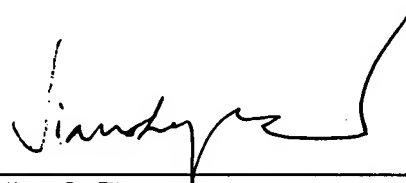
In sum, Applicants respectfully submit that since there is no requisite motivation supporting the modification of the cited references and since the cited references when combined still fails to suggest or teach all of the limitations of invention as currently claimed, the Applicant's invention is not obvious. As such, Applicants respectfully request withdrawal of the 35 U.S.C. §103(a) rejection over claims 1-11.

### **CONCLUSION**

In view of the foregoing and in conclusion, the Applicant submit that the rejections set-forth in the Office Action have been overcome, and that all pending claims are now in conditions for allowance.

Should the Examiner believe that a discussion with Applicants' representative would further the prosecution of this application, the Examiner is respectfully invited to contact the undersigned. The Commissioner is hereby authorized to charge any other fees which may be required under 37 C.F.R. §§1.16 and 1.17, or credit any overpayment, to Deposit Account No. 50-2965.

Respectfully submitted,



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**MATERIAL SAFETY DATA SHEET****MANGANESE CITRATE**  
**CODE #2569**

EMERGENCY PHONE NUMBER  
314.428.4300 (Monday thru Friday, 8 a.m. – 5 p.m. CST)  
-OR-  
314.313.4374 (after business hours)

EFFECTIVE DATE:  
07/08/02

**SECTION 1****PRODUCT IDENTIFICATION**

CHEMICAL NAME:	Manganese Citrate		
SYNONYMS:	Citric Acid, Manganese Salt (2.3)		
CHEMICAL FORMULA:	$Mn_3(C_6H_5O_7)_2 \cdot 9H_2O$		
FORMULA CAS NO.:	10024-66-5	Mol. Wt.	705.1
HAZARDOUS INGREDIENTS:	Manganese Citrate		

**SECTION 2****SUMMARY OF HAZARDS**

PRECAUTIONARY MEASURES:	WARNING! Chronic inhalation hazard. Avoid prolonged or repeated inhalation of dust. Keep container closed. Use only with adequate ventilation.
EMERGENCY FIRST AID:	If dust inhaled, remove to fresh air

**SECTION 3****PHYSICAL DATA**

APPEARANCE:	Pale pink
ODOR:	Odorless
SOLUBILITY:	Very slightly soluble
MELTING POINT:	Greater than 150°C

**SECTION 4****FIRE AND EXPLOSION HAZARD DATA**

FIRE:	If ignited this product supports combustion
EXPLOSION:	Not considered to be an explosion hazard
FIRE EXTINGUISHING MEDIA:	Carbon dioxide or dry chemical extinguisher advised.

## **SECTION 5**

## **REACTIVITY DATA**

STABILITY: Stable under ordinary conditions of use and storage.

CONDITION/MATERIAL TO AVOID: Strong oxidizing agents.

HAZARDOUS DECOMPOSITION  
PRODUCTS: Oxides of Manganese and Carbon.

HAZARDOUS POLYMERIZATION: This substance does not polymerize

## **SECTION 6**

## **HEALTH HAZARD INFORMATION**

### **A. EXPOSURE/HEALTH EFFECTS**

INHALATION: Can cause mild to moderate irritation depending on the duration of contact. Acute symptoms of exposure: Pulmonary effects, consisting of dyspnea, shallow respiration and fever which mimic metal fume fever. Physical irritation of eyes and throat. Cold-like symptoms, chills and muscle aches, dryness of the mouth.

INGESTION: Ingestion can produce gastrointestinal irritation.

SKIN CONTACT: Acute symptoms of exposure: Red, dry skin  
Chronic symptoms of exposure: Dermatitis

EYE CONTACT: Acute symptoms of exposure: Redness, tear production of eyes.

TARGET EFFECTS: Neurotoxin, may affect the respiratory system.

CHRONIC EXPOSURE: INHALATION: Central nervous system: symptom may appear after 1-2 years of elevated exposure.  
EYES: Conjunctivitis and corneal damage from irritant dusts.  
SKIN: Dermatitis

### **B. FIRST AID**

INHALATION: Remove to fresh air. Treat symptoms. Get medical attention for any breathing difficulty.

INGESTION: If swallowed and the person is conscious, drink water and induce vomiting. Call a physician.

SKIN CONTACT: Wash thoroughly with soap and water. A shower is recommended if significant exposure occurs.

EYE CONTACT: Immediately flush for at least 15 minutes while holding eyelids open. If symptoms develop, consult physician.

CAUTION: IF UNCONSCIOUS, HAVING TROUBLE BREATHING OR IN CONVULSIONS, DO NOT INDUCE VOMITING OR GIVE WATER.

C. TOXICITY DATA None found

#### **SECTION 7**

#### **LEAK/SPILL INFORMATION**

SPILL CONTROL & RECOVERY: Sweep or shovel material into waste disposal container. Flush area with water.

DISPOSAL: Dispose of in accordance with applicable federal, state, and local regulations.

#### **SECTION 8**

#### **OCCUPATIONAL CONTROL MEASURES**

AIRBORNE EXPOSURE LIMITS: None established

VENTILATION SYSTEMS: General ventilation is recommended.

PERSONAL RESPIRATORS: Where airborne concentrations may exceed OSHA/ACGIH permissible air concentrations, the minimum respiratory protection recommended is a negative pressure air purifying respirator with cartridges that are NIOSH/MSHA approved against dust, fume, and mists having TWA not less than 0.05 mg/cubic meter.

SKIN PROTECTION: Gloves or other protective clothing recommended if skin contact is appreciable. If clothing is contaminated, remove clothing and thoroughly wash the affected area. Launder contaminated clothing before reuse.

EYE PROTECTION: Safety glasses recommended where the possibility of getting dust particles in eyes exist. The availability of an eye wash fountain and safety shower is recommended.

#### **SECTION 9**

#### **STORAGE AND SPECIAL INFORMATION**

Keep in tightly closed container, store in cool, dry, ventilated area. Protect against physical damage.

#### **SECTION 10**

#### **REGULATORY INFORMATION**

SARA III (Superfund Amendments and Reauthorization Act)

Section 313 – This product contains the following substance(s) subject to the reporting requirements of section 313 of the Emergency Planning and Community Right-To-Know-Act of 1986 (40CFR 372):

Manganese Compounds, N450, 100% by wgt.

This information should be included in all MSDS's that are copied and distributed for this material.

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